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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,939	12/20/2000	Cesare Galli	P66004USO	8697

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EXAMINER	
CROUCH, DEBORAH	
ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/647,939	GALLI ET AL.	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-21 and 26-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-21 and 26-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *132*.

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Applicant's arguments filed February 1, 2008 have been fully considered but they are not persuasive. The amendment has been entered. Claims 19-21 and 26-32 are pending.

The declaration by Cesare Galli has been considered and is persuasive.

Applicant's arguments in view of the declaration by Cesare Galli have overcome the rejection under 35 U.S.C. § 112, first paragraph that the claims lack enablement because mononuclear cells could not support nuclear transfer.

Claims 29-32 are objected to as depending from a rejected claim. Claims 29-32 would be allowable if written in independent form.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-21 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reconstructing a nonprimate mammalian embryo comprising reconstructing a first generation embryo comprising transferring a mononuclear cell isolated from the blood or natural secretion of a nonprimate mammal, or an isolated nucleus of said mononuclear cell, into the cytoplasm of an enucleated nonprimate mammalian oocyte of the same species as the mononuclear cell, activating the oocyte, developing the nonprimate mammalian embryo to a stage where it can be transferred to a uterus, and transferring a cell isolated from the first generation nonprimate mammalian embryo, or an isolated nucleus of said cell into the cytoplasm of an enucleated oocyte from the same species as the mononuclear cell to form a second generation nonprimate mammalian embryo, a method of reconstructing a nonprimate mammalian embryo comprising reconstructing a first generation nonprimate mammalian embryo comprising transferring a nonprimate mammalian mononuclear cell from the blood

or natural secretion of a nonprimate mammal or a nucleus isolated from a mononuclear cells to an enucleated nonprimate mammalian oocyte of the same species as the mononuclear cells, preparing fetal fibroblast cultures from the first generation embryo and transferring cells from said fetal fibroblast cultures to an enucleated oocyte of the same species as the mononuclear cell to form a second generation embryo, where the fetal fibroblasts are genetically modified, and permitted the development of the nonprimate mammalian embryo to term, and methods of producing a nonprimate mammal comprising developing to term the second generation nonprimate mammalian embryo, does not reasonably provide enablement for a method of reconstructing a mammalian embryo comprising reconstructing a first generation embryo comprising transferring a mononuclear cell isolated from the blood or natural secretion of a mammal, or an isolated nucleus of said mononuclear cell, into the cytoplasm of an enucleated oocyte, activating the oocyte, developing the embryo to a stage where it can transferred to a uterus, and transferring a cell isolated from the first generation embryo, or an isolated nucleus of said cell into the cytoplasm of an enucleated oocyte to form a second generation embryo, a method of reconstructing a mammalian embryo comprising reconstructing a first generation embryo comprising transferring a mononuclear cell from the blood or natural secretion of a mammal or a nucleus isolated from a mononuclear cells to an enucleated oocyte, preparing fetal fibroblast cultures from the first generation embryo and transferring cells from said fetal fibroblast cultures to an enucleated oocyte suitable recipient to form a second generation embryo, where the fetal fibroblasts are genetically modified, and permitted the development of the embryo to term, and methods of producing a mammal comprising developing to term the second generation embryo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are not enabled because at the time of filing, the art regarded the production of nonprimate mammals by nuclear transfer as not enabled. The cloning of monkeys by nuclear transfer had been successful when embryonic cells were the nuclear donors, not when somatic cells were used as nuclear donor (Mitalipov, abstract). Mitalipov further states, clearly, that somatic cell cloning, as is part of the present methods, has not been accomplished in primates (Mitalipov, page 1367, col. 2, parag, 3, lines 1-3). Simerly, states that in rhesus monkey NT units, DNA and microtubule imaging showed disarrayed mitotic spindles with misaligned chromosomes, which resulted in unequal chromosome segregation and aneuploid embryos (page 297, col. 2, parag. 1, lines 5-11). The art, therefore, at the time of filing clearly disclosed the unpredictable nature of nuclear transfer using a primate somatic cell as nuclear donor.

Therefore, at the time of filing, the skilled artisan would have needed to conduct an undue amount of experimentation without a predictable degree of success to implement the invention as claimed.

Applicant argues MPEP 2164.01(b) states only one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim is needed for enablement. Applicant also argues failure to disclose other methods does not render a claim invalid. Applicant argues a single working example in the specification is sufficient for claimed invention is enough to preclude an enablement rejection. These arguments are no persuasive.

In view of applicant's arguments and the declaration by Cesare Galli, a scope of enablement has been given. The art provides evidence that the production of primate embryos and primates by nuclear transfer is unpredictable without an undue amount of experimentation. As a mononuclear is a somatic cell and Mitalipov states somatic cell nuclear transfer has failed in primates, the claimed invention is not enabled for its full

breadth (see above). While the specification need not disclose other NT methods to produce nonprimate mammals, the specific needs to teach NT methods for successful primate production.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19, 26, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over US. Patent 594557 issued March 31, 1999 (Stice) in view of U.S. Patent 6147276 issued November 14, 2008 (Campbell).

Stice teaches a method of nuclear transfer where a mononuclear donor cell or its nucleus is transferred into an MII enucleated oocyte, activating the oocyte and developing the activated oocyte to a stage where it can be transferred tin to a uterus (col. 7, lines 9-26; col. 8, lines 9-17). Stice teaches the production of cattle, buffalo, sheep, goats and pigs (claim 13). Stice does not teach a second nuclear transfer.

However, Campbell teaches a second cloning where a cell from a nuclear transfer embryo is transferred into an enucleated oocyte to for a second embryo (col. 7, lines 55-61). Campbell offers motivation in stating reprogramming can be enhanced so that a greater number of cloned mammals can be obtained (col. 7, lines 62-66).

Thus at the time of the present invention it would have been obvious to the skilled artisan to produce a reconstructed mammalian embryo, especially a cattle, buffalo, sheep, goat or pig embryo, by transfer of a mononuclear cell or it nucleus into an enucleated oocyte, activate the oocyte to produce an embryo, and develop the embryo, where upon, a

serial cloning is performed as taught by Campbell to enhance embryo development. The limitation "can be transferred to a uterus" is seen as any stage, such as the 2-cell stage taught by Stice. An embryo "can be transferred to a uterus" at any developmental time; the limitation does not state the embryo has to be a particular age, size or stage of development.

The combination of prior art cited above in all rejections under 35 U.S.C. 103 satisfies the factual inquiries as set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Once this has been accomplished the holdings in KSR can be applied (*KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. ___, 82 USPQ2d 1385 (2007): "Exemplary rationales that may support a conclusion of obviousness include: (A) Combining prior art elements according to known methods to yield predictable results; (B) Simple substitution of one known element for another to obtain predictable results; (C) Use of known technique to improve similar devices (methods, or products) in the same way; (D) Applying a known technique to a known device (method, or product) ready for improvement to yield predictable results; (E) "Obvious to try" - choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success; (F) Known work in one field of endeavor may prompt variations of it for use in either the same field or a different one based on design incentives or other market forces if the variations are predictable to one of ordinary skill in the art; (G) Some teaching, suggestion, or motivation in the prior art that would have led one of ordinary skill to modify the prior art reference or to combine prior art reference teachings to arrive at the claimed invention." In the present situation, rationales A, B, F and G are applicable. The claimed method was known in the art at the time of filing as indicated by Stice and Campbell. Thus, the teachings of the cited prior art in the obviousness rejection above provide the requisite teachings and motivations with a clear, reasonable expectation. The cited prior art meets the criteria set forth in both

Graham and KSR.

Claims 20, 21, 27, 28, 31 and 32 are free of the prior art. At the time of filing the prior art did not teach or suggest a method of reconstructing a mammalian embryo comprising reconstructing a first generation embryo comprising transferring a mononuclear cell from the blood or natural secretion of a mammal to a suitable recipient, preparing fetal fibroblast cultures from the first generation embryo and transferring cells from said fetal fibroblast cultures to a suitable recipient to form a second generation embryo, and where the fetal fibroblasts.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is 571-272-0727. The examiner can normally be reached on M-Fri, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch, Ph.D./
Primary Examiner, Art Unit 1632

June 3, 2008